Participating in the Webinar

All attendees will be muted and will remain in "Listen Only Mode".

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.
ACG Virtual Grand Rounds
Join us for upcoming Virtual Grand Rounds!

Week 16 – Thursday, April 20, 2023
Quality Indicators for Capsule Endoscopy and Deep Enteroscopy: An ACG and ASGE Joint Publication
Faculty: Jonathan A. Leighton, MD, FACG
Moderator: Carol E. Semrad, MD, FACG
At Noon and 8pm Eastern

Week 17 – Thursday, April 27, 2023
Gut Directed Hypnotherapy for IBS: What Gastroenterologists and Patients Should Know
Faculty: Olafur Palsson, PsyD
Moderator: Megan E. Riehl, PsyD, MA
At Noon and 8pm Eastern

Visit gi.org/ACGVGR to Register

ACG 2023
October 20-25, 2023
Vancouver, Canada

Save the Date!
Be sure your passport is up to date!
CASE PRESENTATION

- AH a 15-year-old female living with her parents
- Presented with recurrent vomiting, epigastric pain, weight loss and generalized body weakness of three months duration and recurrent paleness of one month
- Vomits food 20-30 minutes after feed
- Vomiting is triggered by feeds and vomits an average of 5 to 6 times daily
- Had associated abdominal pain and frequent regurgitation
- Weight on admission was 39kg
OTHER ASPECT OF HISTORY

• She first visited a Secondary level hospital five years ago, but no significant diagnosis was made and was then referred to a tertiary hospital in another state and later to UCTH 3 yrs ago where the first upper GI endoscopy was done, endoscopically the oesophagus, stomach and duodenum appeared normal
• She was managed for GERD with significant improvement but was lost to follow up
• She is the first of two children
• There is a family history of atopy

EXAMINATION FINDINGS

• GENERAL PHYSICAL EXAMINATION : NAD

• ANTHROPOMETRY on admission: weight=39kg, height=1.71m, BMI=13.3kg/m², weight for age - at 0 z-score, height for age - above +1 z-score, BMI for age - below -3 z-score

• DIGESTIVE SYSTEM - Good oral hygiene with good dentition. Abdomen: NAD

• OTHER SYSTEMS: essentially normal
INVESTIGATIONS WITH RESULTS

• Upper GI endoscopy with biopsies of the oesophagus, stomach and duodenum taken. This was suggestive of eosinophilic oesophagitis on histology.
• PCV before admission - 29% and PCV on discharge - 32%
• Hepatitis screening: HBsAg and HCV - non-reactive
• HIV screening: Negative
• LFT and E/U/Cr - were within normal range
• FBC - RBC morphology - Anisocytosis +ve, Microcytosis +ve, Hypochromasia +ve, Neutrophil - 36%, Lymphocyte - 60%, Eosinophil - 4%, Monocyte - 0%, Basophils - 0%
INVESTIGATIONS WITH RESULTS

- Abdominal USS - No significant finding
- Barium Swallow, meal and follow through - No significant findings
- ESR - within normal range
- H. pylori stool antigen test: negative
- Stool microscopy for parasite: negative
- Contrast CT of the abdomen: Normal

TREATMENT AND PROGRESS

- She was admitted into the Paediatric medical ward
- 4hrs into admission she vomited thrice, vomiting was provoked by feeds and contained undigested food
- Vomits 5-6 times daily in the first week of admission
- She was commenced on; PPI 40mg once daily for two months
- Oral corticosteroid (Prednisolone) was commenced when there was no improvement with PPI
- Swallowed Fluticasone @ 220mcg twice daily for six months
- Budesonide inhaler- not available
- Vitamin B12 10mg once daily for two weeks
- Iron supplement was prescribed on discharge
TREATMENT AND PROGRESS

- Counselling to eliminate milk, peanuts, fish, eggs, bread from diet
- She showed remarkable improvement with no vomiting before discharge
- Anthropometry on discharge: weight=43kg, height=1.71m, BMI=14.4kg/m², weight for age - between +2 and +1 z-score, height for age - between +2 and +1 z-score, BMI for age - between -2 and -3 z-score
- Continued on outpatient management
- Had a repeat upper GI endoscopy after discharge
Eosinophilic Esophagitis in Pediatrics

Prasanna K. Kapavarapu MD
Assistant Professor of Clinical Pediatrics
Associate Program Director, Pediatric Neurogastroenterology & Motility Fellowship
Children's Hospital of Philadelphia
Perelman School of Medicine at the University of Pennsylvania

Layout of today’s presentation

- **Background:** History, Definition, Epidemiology
- **Pathophysiology:** Genetics, Environmental factors
- **Clinical presentation:** Symptoms, Coping behaviors
- **Diagnosis:** Endoscopy
- **Management:** Nutritional, Pharmacotherapeutics
- **Future directions in EoE**
Background: History

1970’s: description in case reports
- 1978: case report of eosinophilic esophagitis in Achalasia
- 1982: case report of eosinophilic esophagitis in Reflux

1990’s: further description in case series
- 1993: 12 patients with dysphagia had intraepithelial eosinophilic esophagitis
- 1994: 10 patients with dysphagia had intraepithelial eosinophilic esophagitis

1995: RECOGNITION as a distinct entity - Eosinophilic Esophagitis (EoE)

Patient population:
- 10 children, 8mth to 12yrs age, longstanding GERD
- Anti-reflux medications (n=10), s/p Nissen fundoplication (n=6)

<table>
<thead>
<tr>
<th>N=10</th>
<th>Baseline</th>
<th>Elemental formula for 6 weeks</th>
<th>Open food challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>GERD</td>
<td>Resolution (n=8) Improvement (n=2)</td>
<td>Return of symptoms</td>
</tr>
<tr>
<td>EGD: Intraepithelial eosinophils</td>
<td>41/hpf (median)</td>
<td>0.5/hpf (median)</td>
<td>Not performed</td>
</tr>
</tbody>
</table>

Kelly et al, Gastro 1995
**Background: History**

- 1995: RECOGNITION as a distinct entity - Eosinophilic Esophagitis (EoE)
- Patient population:
  - 10 children, 8mth to 12yrs age, longstanding GERD

For the FIRST time:
FOOD was implicated in esophageal inflammation

<table>
<thead>
<tr>
<th>Eosinophils</th>
<th>(median)</th>
<th>Baseline</th>
<th>(median)</th>
<th>Improvement</th>
<th>Not performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOSI/Intraepithelial</td>
<td>41/hpf</td>
<td>0.5/hpf</td>
<td>(median)</td>
<td>(median)</td>
<td>performed</td>
</tr>
</tbody>
</table>

For the FIRST time:
FOOD was implicated in esophageal inflammation

Kelly et al, Gastro 1995

**Background: Definition**

- Eosinophilic Esophagitis (EoE) represents a chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.

Liacouras et al, J Allergy Clin Immunol 2011
Background: Epidemiology

- EoE: Epidemiology
  - Incidence: 5 to 10 per 100,000
  - Prevalence: 0.5 to 1 per 1000

- EoE: Familial susceptibility
  - First degree relative: 1.8%
  - Parent: 0.6 to 2.4%
  - Sibling: 1.3 to 3.5%
  - Monozygotic twins: 40%
  - Dizygotic twins: 30%

Dellon et al, Gastro 2018; James et al, Clinic Rev Allergy Immunol 2018; Reed et al Med Clin N Am 2019
Pathophysiology: Genetics

- EoE genetic risk loci: 6
- EoE candidate risk genes: 13
- EoE risk genes expressed in various cell types (esophageal epithelium, fibroblast, immune cells)
- Risk of EoE in individuals with highest decile of genetic burden compared to lowest decile of genetic burden: 12-fold risk

Kottyan et al, J Allergy Clin Immunol 2021

Pathophysiology:

Biedermann et al, Nature Reviews: Gastro & Hepatol 2023
Pathophysiology

Triggers:
- Diet
- Environment

Biedermann et al, Nature Reviews: Gastro & Hepatol 2023

Hirano et al, Gastro 2020
Pathophysiology: Environmental factors

- 68% of children with EoE have atopy: Out of 620 children with EoE
  - Asthma: 50%
  - Allergic Rhinitis: 61%
  - Atopic dermatitis: 21%
  - Food allergy/anaphylaxis 5.7%

Pathophysiology: Relationship between EoE and Atopy

<table>
<thead>
<tr>
<th>Author/Year [Ref]</th>
<th>No. EoE Patients</th>
<th>Age (y)</th>
<th>Asthma</th>
<th>AR</th>
<th>AD</th>
<th>FA (Anaphylaxis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spergel et al. 2008</td>
<td>620</td>
<td>9.1 ± 3.1</td>
<td>50%</td>
<td>61%</td>
<td>21%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Assaf et al. 2002</td>
<td>89</td>
<td>6.2 ± 4.8</td>
<td>39%</td>
<td>30%</td>
<td>19%</td>
<td>9.0%</td>
</tr>
<tr>
<td>Sugrnanam et al. 2007</td>
<td>45</td>
<td>3 mo to 16 y</td>
<td>66%</td>
<td>93%</td>
<td>55%</td>
<td>24.0%</td>
</tr>
<tr>
<td>Guajardo et al. 2002</td>
<td>39</td>
<td>8 ± 12</td>
<td>38%</td>
<td>64%</td>
<td>25%</td>
<td>23.0%</td>
</tr>
<tr>
<td>Roy-Ghanta et al. 2008</td>
<td>23</td>
<td>18 to 57</td>
<td>26%</td>
<td>78%</td>
<td>4%</td>
<td></td>
</tr>
</tbody>
</table>
EoE: Clinical Presentation

Clinical presentation: Symptoms
• Varies by AGE

<table>
<thead>
<tr>
<th>Table 3. Symptoms Suggestive of Eosinophilic Esophagitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Feeding aversion/intolerance</td>
</tr>
<tr>
<td>Vomiting/regurgitation</td>
</tr>
<tr>
<td>“GERD refractory to medical management”</td>
</tr>
<tr>
<td>“GERD refractory to surgical management”</td>
</tr>
<tr>
<td>Food impaction/foreign body impaction</td>
</tr>
<tr>
<td>Epigastric abdominal pain</td>
</tr>
<tr>
<td>Dysphagia</td>
</tr>
<tr>
<td>Failure to thrive</td>
</tr>
</tbody>
</table>

Noel et al, NEJM 2004; Furuta et al Gastro 2007
### Clinical presentation: Symptoms - Coping Behaviors

#### Table 1: Eating Behaviors in Pediatric Patients With Eosinophilic Esophagitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Infants or toddlers</th>
<th>Grade school</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of meals</td>
<td>Mealtimes longer than sibling or rest of family; often leaves and comes back to the table; grazes on small volumes of liquid or food</td>
<td>Mealtimes longer than friends; returns from school with full lunchbox</td>
<td>Avoids social dining due to prolonged mealtimes or fear of food getting stuck</td>
</tr>
<tr>
<td>Coping behaviors</td>
<td>Preference for liquids and soft foods over solid foods</td>
<td>Use of large amounts of dips, saucers, or liquids to help swallowing; may have narrow range of preferred foods</td>
<td>Always needs water bottle or liquids with meals</td>
</tr>
<tr>
<td></td>
<td>Pockets food in cheek for prolonged periods and/or spills food out; dips foods in liquids</td>
<td>Prolonged chewing of food before swallowing</td>
<td>Prefers a soft-textured diet</td>
</tr>
<tr>
<td>Food selection</td>
<td>Difficulty advancing diet from pureed baby food; demonstrates feeding refusal or fussy behavior during meals</td>
<td>Difficulty to refusal to expand diet with new flavors, types of foods, or textures</td>
<td>Avoidance of certain food textures, specifically meats, bread, rice, raw fruits, and vegetables</td>
</tr>
</tbody>
</table>

Hirano et al, Gastro 2020

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### EoE: Diagnosis

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Background: Diagnostic criteria

Table 2. EoE Diagnostic Criteria

- Symptoms of esophageal dysfunction
  - Concomitant atopic conditions should increase suspicion for EoE.
  - Endoscopic findings of rings, furrows, exudates, edema, stricture, narrowing, and crepe paper mucosa should increase suspicion for EoE.
- $\geq 15$ eos/hpf ($\sim 60$ eos/mm$^2$) on esophageal biopsy
  - Eosinophilic infiltration should be isolated to the esophagus.
- Assessment of non-EoE disorders that cause or potentially contribute to esophageal eosinophilia

Diagnosis: Differential diagnosis

Table 3. Conditions Associated With Esophageal Eosinophilia

- Eosinophilic esophagitis
- Eosinophilic gastritis, gastroenteritis, or colitis with esophageal involvement
- GERD
- Achalasia and other disorders of esophageal dysmotility
- Hypereosinophilic syndrome
- Crohn's disease with esophageal involvement
- Infections (fungal, viral)
- Connective tissue disorders
- Hypermobility syndromes
- Autoimmune disorders and vasculitides
- Dermatologic conditions with esophageal involvement (ie, pemphigus)
- Drug hypersensitivity reactions
- Pill esophagitis
- Graft vs host disease
- Mendelian disorders (Marfan syndrome type II, hyper-IgE syndrome, PTEN hamartoma tumor syndrome, Netherton syndrome, severe atopic metabolic wasting syndrome)
Diagnosis of EOE

- History
  - Symptoms
  - Coping behaviors
  - Concomitant atopy
- Lab tests: if considering other diagnosis
- Upper GI study to assess for narrowing (rule out anatomic causes of dysphagia)
- Endoscopy

Diagnosis: Endoscopy Findings in EoE

- Normal Esophagus
- Furrowing
- White Plaques
- Rings
- Narrow Caliber
**Diagnosis: EoE Histopathology**

- Eosinophilic Infiltrates (>15 eos/hpf)
- Basal Cell Hyperplasia (BCH)
- Lamina Propria Fibrosis
- Dilated Intracellular Spaces (Spongiosis)

**EoE: Treatment**
EoE Treatment: RATIONALE

• Manage symptoms

• Prevent worsening esophageal dysfunction

• Avoid fibrosis, strictures, and food impactions

Dellon et al, Gastroenterol 2018

EoE Treatment: GOALS of treatment

• GOALS: Minimize
  • Symptoms
  • Histopathologic features
  • Endoscopic features

• Therapy
  • Effective: White center
  • Ineffective: Outer black circle

• Composite approach
  • 1: Anti-inflammatory therapy: improves symptoms and histopathology features
  • 2. Dilation: improves symptoms and endoscopic features

Hirano et al, Gastro 2020
EoE Treatment: Algorithm – up to 2018

Furuta et al Gastro 2007; Liacouras et al, J Allergy Clin Immunol 2011; Papadopoulou et al, JPGN 2014

EoE Treatment: Algorithm – up to 2018

Furuta et al Gastro 2007; Liacouras et al, J Allergy Clin Immunol 2011; Papadopoulou et al, JPGN 2014
EoE Treatment: Algorithm – CURRENT after 2018

Clinical presentation suggestive of EoE

EGD with biopsy

Esophageal eosinophilia ≥ 15 eos/hpf (~60 eos/mm²)

Evaluate for non-EoE disorders that cause or potentially contribute to esophageal eosinophilia

Eosinophilic esophagitis

Figure 1. Updated EoE diagnostic algorithm.

No trial with PPI
PPI-REE: not used anymore

Dellon et al, Gastro 2018
**EoE Treatment: Elimination diet**

Types of Elimination diet
- 6 food elimination diet
- 4 food elimination diet
- 1 food elimination diet

Approach:
- Step-down approach
- Step-up approach

---

**Fig. 1.** Step-down approach for diet elimination therapy. EGD, esophagogastroduodenoscopy.
EoE Treatment: Elimination diet: Step-up approach

Fig. 2. Step-up approach for diet elimination therapy.

Ruffner et al, Pediatr Clin N Am 2021

Figure 1. Diagram outlining the order of food reintroduction in responders. Single foods reintroduced every 8 weeks in 4-FED responders starting with soy, egg, wheat, and milk. Inflammation-inducing trigger foods removed followed by a normal baseline EGD demonstrating remission of inflammation before the next food reintroduction. 4-FED, 4-food elimination diet.

Kagalwalla et al, Clin Gastro Hepatol 2017
Six food elimination diet vs. elemental diet
(NO milk, egg, soy, wheat, peanut/nuts, seafood)

- 60 children
  - 35 on Six-Food elimination diet
  - 25 on Elemental diet
- Repeat endoscopy-6 weeks later
  - 74% of Six-food elimination diet < 10 eos/hpf
  - 88% of Elemental diet had <10 eos/hpf

Kagalwalla et al, Clin Gastro Hepatol 2006

Four food elimination diet
(NO milk, egg, soy, wheat)

- 78 children in US multi-center pediatric trial
- 8 weeks elimination of 4 foods and 8 weeks addition of single food
- 63% response rate (<15 eos/hpf)
  - Causative foods
    - cow’s milk (85%)
    - egg (35%)
    - wheat (33%)
    - soy (19%)

Kagalwalla et al, Clin Gastro Hepatol 2017
One food elimination diet – POSSIBLE 1st line of therapy (NO milk)

- **Pediatrics**: n=41, 6-13yrs age
- Histological remission in 51% (n=21) after 8 weeks

### Table 4. Outcomes of 1FED on Histologic, Endoscopic, and Clinical Metrics in Pediatric EoE

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Responder&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Nonresponder&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGD to assess histologic response to CM elimination, n</td>
<td>41</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Resolution of ≥1 endoscopy findings, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24 (59)</td>
<td>13 (62)</td>
<td>11 (55)</td>
</tr>
<tr>
<td>Resolution of all endoscopic findings, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10 (24)</td>
<td>7 (33)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Resolution of ≥1 symptoms, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25 (61)</td>
<td>19 (71)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Resolution of all symptoms, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12 (29)</td>
<td>4 (19)</td>
<td>8 (40)</td>
</tr>
</tbody>
</table>

CM: cow’s milk; EGD: esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; 1FED, 1-food elimination diet.
<sup>a</sup>A responder was defined by a peak eosinophil count fewer than 15 eosinophils per high power field on esophageal biopsy specimens after a 1FED.
<sup>b</sup>The percent denominator is the column total.

Wechsler et al, Clin Gastro Hepatol 2022

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One food elimination diet – POSSIBLE 1st line of therapy (NO milk)

- **Adults**: 1-food vs 6-food elimination diet
  - 1-food: n=67, 34% responders
  - 6-food: n=62, 40% responders

- Out of the 1-food non-responders who proceeded to 6-food - 43% remission
- Out of the 6-food non-responders who proceeded to topical steroids - 82% remission

Kleiner et al, Lancet Gastroenterol Hepatol 2023
EoE Treatment: Nutritional therapy

- Potential first line therapy for EoE
- Safe, minimal side effects
- 30% of patients will respond to high dose PPI therapy
  - 2mg/kg/day
- Anti-inflammatory role in the esophageal epithelium

Franciosi et al, J of Asthma and Allergy 2022
**EoE Treatment: PPI**

PPI: Anti-inflammatory mechanism of action
- Eotaxin-3 is potent eosinophil chemoattractant drawing eosinophils
- PPI reduces IL-4 stimulated eotaxin-3 expression
- PPI reduces IL-13 signaling
- PPI has an anti-inflammatory effect independent of the antisecretory effect on parietal cells

Franciosi et al, *J of Asthma and Allergy* 2022

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**EoE Treatment: Swallowed steroids**

- A mainstay of EoE treatment in adults and children: 50-85% effective
- Budesonide slurry (concentration matters):
  - 5 packets Splenda, 1 tsp honey, 1 tsp applesauce, etc.
- Flovent Spray:
  - Spray and swallow
  - Technique matters: NOTHING to eat, drink, rinse for 30 minutes


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American College of Gastroenterology
**EoE Treatment: Swallowed steroids – Side Effects**

- **Adrenal Suppression**
  - Out of 106 patients on topical steroids, only 5 patients had a low morning cortisol
  - All 5 of these patients were on inhaled topical steroids as well

- Treatment is not associated with anthropomorphic growth changes (study over 1 year)

- Thrush/candida (resolves with therapy)

_Hsu et al, Pediatric Allergy Immunol 2017_

---

**EoE Treatment: Biologics - DUPILUMAB**

**FDA NEWS RELEASE**

**FDA Approves First Treatment for Eosinophilic Esophagitis, a Chronic Immune Disorder**

For Immediate Release:
May 20, 2022

Today, the U.S. Food and Drug Administration approved Dupixent (dupilumab) to treat eosinophilic esophagitis (EoE) in adults and pediatric patients 12 years and older weighing at least 40 kilograms (which is about 88 pounds).

Today's action marks the first FDA approval of a treatment for EoE.

_FDA News release, May 2022_
EoE Treatment: Biologics - DUPILUMAB

Mechanism of action:

• Anti-IL-4 receptor-α (IL-4Rα)

• Inhibits IL-4 and IL-13 signaling a key pathway for Type inflammation in EoE

Rothenberg et al, J Allergy Clin Immunol 2022
EoE Treatment: DUPILUMAB

Current approved use:

Current Approved Use for Dupilumab

- Atopic dermatitis: Adult and pediatric patients age 6 months and older with moderate-to-severe atopic dermatitis whose diseases are not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- Asthma: Add-on maintenance treatment of adult and pediatric patients age 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid-dependent asthma.
- Chronic rhinosinusitis with nasal polyposis: Add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis.
- EoE: for the treatment of adult and pediatric patients 12 years and older, weighing at least 40 kg, with EoE.

Prurigo nodularis: For the treatment of adult patients with prurigo nodularis.

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Clinical Scenarios Suggesting the Use of Dupilumab for Eosinophilic Esophagitis

Contexts Where First Line Use Should Be Considered

- Patients with multiple comorbid atopic conditions that include
  - Moderate, persistent, or difficult to control asthma
  - Moderate, persistent, or difficult to control atopic dermatitis
  - Difficult to control chronic sinusitis with nasal polyps

- Patients with a strong preference to avoid dietary restriction or topical swallowed steroids

Context when dupilumab can be considered as step up therapy

- Eosinophilic Esophagitis that is difficult to treat
- Patient with frequent use of rescue therapies
  - Oral systemic steroids
  - Esophageal dilations
- Patients with severe diet restriction or requiring amino acid formula
- Patients with clinically significant esophageal strictures or narrow caliber esophagus
- Patients refractory to current therapy
  - Due to continued symptoms
  - Due to persistent abnormal esophageal inflammation
  - Due to adverse effects of current therapy
  - Due to intolerance of current therapy
  - Due to inability to adhere to current therapy
- Patients with adverse effects to current therapy

Aceves et al, Ann Allergy Asthma Immunol 2023
EoE Treatment: DUPILUMAB

Most common side effects:
- Injection site reactions
- Upper respiratory tract infections
- Joint pain
- Herpes viral infections

FDA News release, May 2022

EoE Treatment: DUPILUMAB

- Dupilumab is contraindicated in patients with known hypersensitivity to dupilumab or any of its inactive ingredients.

- Dupilumab carries warnings and precautions, including ones addressing potential development of allergic reactions, conjunctivitis, keratitis, or joint pain; use in patients with certain parasitic infections; and use in conjunction with live vaccinations.

FDA News release, May 2022
EoE Treatment: Esophageal dilation

- Indications:
  - Esophageal strictures
  - Narrow caliber esophagus
  - Persistent dysphagia/food impaction
- Equipment: Balloon dilators or Bougie
- Complications:
  - Chest pain up to 3 days
  - Esophageal perforation (minimal)
- Immediate symptomatic improvement in majority of patients. However, symptoms recur in majority of patients
- Need for effective long-term treatment of EoE with nutritional or diet manipulations

Lucendo et al, Curr Opin Gastroenterol 2018

EoE Treatment: REFRACTORY EoE

Box 1 | Proposed definition of refractory EoE

After a PPI trial, and following treatment with either topical corticosteroids or dietary elimination, refractory EoE can be defined as:
- Persistent oesophageal eosinophilia (≥15 eos/hpf)
- Incomplete resolution of the primary presenting symptoms
- Incomplete resolution of endoscopic findings of EoE

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high-power field.

Dellon et al, Nature Reviews 2017

Box 2 | Potential explanations for non-response

For topical corticosteroids:
- Non-adherence
- Dose too low
- Inappropriate administration
- Suboptimal formulation (low dwell time)
- Persistent allergen exposure
- Superimposed infection (for example, with Candida spp. or herpes simplex virus)
- Stricture causing persistent symptoms
- Incorrect diagnosis of EoE

For dietary elimination:
- Non-adherence
- Inadvertent contamination
- Correct trigger, or triggers, not eliminated and/or persistent allergen exposure
- Stricture causing persistent symptoms
- Incorrect diagnosis of EoE

EoE, eosinophilic oesophagitis.
EoE Treatment: REFRACTORY EoE

Possible non-response to a first-line EoE treatment
- Evaluation of non-response
  - Adherence?
  - Dose, formulation, delivery?
  - Antigen exposure and/or cross-contamination?
  - Infection or stricture?
  - Correct diagnosis?
- Confirmed EoE non-response
  - Initial treatment with topical steroids
    - Maximize steroids
      - Increase dose
      - Change formulation
      - Different topical steroids
    - Non-response
    - Dietary elimination
    - Maximize diet
      - More restrictive diet
      - Improved adherence
    - Non-response
    - Topical steroids
- Continued EoE non-response
  - Systemic steroids
  - Dilation programme
  - Elemental formula
  - Clinical trials
  - Immunosuppressors
  - Combination treatment?
  - Leukotriene antagonists
  - Biologic(s)? (future)

Dellon et al, Nature Reviews 2017

EoE Treatment: Long term SURVEILLANCE

- No standard guidelines for long term endoscopic monitoring in asymptomatic EoE. BUT EoE can still be active without symptoms
- Recommend CLOSE FOLLOW UP

Bon et al, United European Gastroenterol J 2022
EoE Treatment: After therapy is initiated

- One must have a repeat endoscopy to truly know what is going on in the esophagus
  - Whatever plan is patient must be followed with an EGD
  - Patient can still have esophageal eosinophils without symptoms
  - Patients might need multiple endoscopies over time (depends on therapy)

Future directions in EoE
Future of EoE: New techniques for testing

• String test
• Sponge test

Cytosponge test: Adults

Figure 3. Correlation of eosinophil counts per HPF on matched patients for cytosponge and biopsy specimens. Spearman’s Rho is reported.

Figure 4. Receiver operator characteristic curve for accuracy of cytosponge compared to a threshold of 15 eos/HPF in endoscopic biopsy for identification of active eosinophilic esophagitis. AUC, area under the curve.
Future of EoE: New techniques for testing

• String test: Pediatrics
  - Ackerman et al, AJG 2019

Future of EoE: New techniques for testing

• Trans Nasal Endoscopy (TNE)
  - No sedation/anesthesia
  - Local anesthetic spray
  - Distraction with Virtual Reality (VR) headsets
  - Patients have to be a little older for co-operation
  - Cost effective

Nguyen et al, Clin Gastroenterol Hepatol 2019
Future of EoE: New techniques for testing

EndoFLIP in EoE

• Characterizing EoE: Fibrostenotic or Inflammatory
• Better characterization of patients at time of initial endoscopy can assist in assessing the esophageal distensibility and in developing follow up plan
Future of EoE: New techniques for testing

- EndoFLIP in EoE

Menard-Katcher et al, AJG 2016
EoE: Case scenarios

Case # 1

Take away points:

• Presentation: Adolescent with GI symptoms (vomiting, abdominal pain, poor weight)
• History: Food triggers and Family h/o atopy
• Poor response to PPI
• Good response to swallowed steroids and also to targeted food elimination
• Improvement in clinical symptoms and histological features
Case # 2

- Presentation: 3yr old male with c/o poor weight gain

- History:
  - HPI: Limited oral intake, Limited varieties of food, Occasional vomiting
  - Atopy: Reactive airway disease, Eczema
  - Development: Slightly global developmental delay, gets PT/OT
  - PMHx: Ex-26 weeker, had early newborn issues, no chronic issues
  - Family Hx: Mom/Dad have seasonal allergies

- Exam:
  - Growth: Weight <1%, Ht <1%
  - Physical exam: Normal, Skin eczema+, Abdomen NAD

Tests:
- Screening blood work: negative
- Upper GI study: Normal
- Proceed to Endoscopy (EGD)

- EGD:
  - white exudates, loss of vascularity, mild furrowing

- Biopsy:
  - Esophagus: 60eos/hpf, superficial eosinophilic microabscesses
  - Stomach and Duodenum: normal
Case # 2

Treatment:
- Discuss options: Elimination diet vs PPI vs Steroids or a combination
- Already has food refusal behaviors and poor weight gain
- Parents opted: PPI + Swallowed steroids

After 8 weeks:
- Symptoms:
  - Started to improve, working with Nutrition to optimize food intake
  - Improved growth parameters
- Repeat Endoscopy: Improved both endoscopically and histologically

Take away points:
- Presentation: Toddler with food refusal behavior and poor weight gain
- History: Environmental factors (primie), H/o Atopy in patient and Family
- Endoscopy: endoscopic and histologic changes of EoE
- Discuss treatment options with parents/caregivers
- Good response to PPI and swallowed steroids
- Mindful of further restricting food in a patient with food refusal behaviors
Case # 3

• Presentation: 17yr old male presented to Emergency Room with food impaction after eating a piece of chicken

• History:
  • HPI: Coping behaviors: long time to finish meals, drinks a lot of water along with meals, avoids eating dry foods
  • PMH: IgE mediated peanut allergy
  • Family Hx: H/o adult in the family needing dilations of esophagus

• Exam: NAD

Tests:
• Screening blood work: negative
• EGD: emergent endoscopy
  • Food noted in the esophagus
  • White exudates
  • Narrow caliber
  • Friable mucosa

• Biopsy:
  • Esophagus: 75eos/hpf, lamina propria fibrosis
  • Stomach and Duodenum: normal
Case #3

Treatment:
• Discuss options: Nutritional vs PPI vs Steroids
• Patient and family opted: Swallowed steroids

After 8 weeks:
• Symptoms: Improved, less coping behaviors
• Repeat Endoscopy: Improved both endoscopically and histologically

Take away points:
• Presentation: Adolescent with food impaction needing emergent endoscopy
• History: Peanut allergy, Coping behaviors, Family h/o esophageal dilations
• Good response to swallowed steroids
• Improvement in clinical symptoms and histological features
• Mindful of long-term compliance
Conclusions

- The gold standard for diagnosis of EoE is an endoscopy with biopsy
- Clinicians need to have a high index of suspicion for diagnosing EoE because symptoms are vague
- Therapeutic options include diet modifications, proton pump inhibitors and swallowed steroids
- FDA recently approved Dupilumab in May 2022 for treatment of EoE
- Future non-invasive modalities to assess disease activity are being evaluated

Questions?

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